

REMARKS

A personal Examiner interview was held on August 2, 2006. The interview was attended by Examiner Gary W. Counts; Supervisory Examiner Long Le; and Applicants' representatives, Marcia Morton, Laurence Posorske, and Victoria Silcott. Applicants thank Examiners Counts and Le for their time and attention.

I. Amendment

Upon entry of the foregoing amendments, claims 2-14 are pending in the application. Claims 2 and 13 are amended.

Claim 2 has been amended to include it in Group III of the Restriction Requirement dated September 27, 2002, drawn to a method for quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a label quantitatively associated with the analyte. As explained by Applicants' representatives during the Interview of August 2nd, claim 2 as amended herein falls within Group III of the Restriction Requirement dated September 27, 2002. Applicants' representatives believe that the Examiners agreed. Support for the amendment to claim 2 can be found, for example, in claims 2 and 3 as originally filed and throughout the specification.

Claim 13 has been amended to ensure clarity. Support for the amendment to claim 13 may be found in the specification at, for example pages 9 and 10.

Applicants submit that the amendments do not constitute new matter. Reconsideration in view foregoing and entry of the amendments is therefore respectfully requested.

II. Claim Rejections Under 35 U.S.C. § 103

The Office Action maintains the rejection of claims 3-10 under 35 U.S.C. § 103(a) as obvious over Park et al., *Homogenous Proximity Tyrosine Kinase Assays*, Anal. Biochem. 269: 94-104 (1999) ("the Park publication") in view of Applicants' prior sale of cross-linked allophycocyanin ("APC") which had not been exposed to strongly chaotropic agents ("Applicants' product"). See Office Action, p. 3. Applicants respectfully traverse the rejections.

The examiner bears the initial burden of establishing a *prima facie* case of obviousness. If the examiner does not satisfy his/her burden, then the applicant is not obligated to submit evidence of nonobviousness. See M.P.E.P. § 2142 at 2100-125 (8th ed., rev. no. 5). In order to satisfy that burden, the examiner must establish: i) the existence of a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary

skill in the art, to modify the reference or to combine reference teachings; 2) the existence of a reasonable expectation of success of making the claimed invention; and iii) that the prior art reference (or references when combined) teach or suggest all of the claim limitations. *See id.*

Applicants respectfully submit that the burden has not been satisfied. It has not been established, for example, that one of ordinary skill in the art would have been motivated to use an allophycocyanin such as SL-APC in the assay disclosed in the Park publication. The assay disclosed in the Park publication used a conventional crosslinked APC ("XL-APC"). The crosslinked APC used in the claimed method ("SL-APC") is made by a different process than XL-APC and was not sold for the purpose of using it in the assay of the Park publication, as stated in the Declaration of Mark Wesley Moss, submitted to the USPTO on September 29, 2005 ("the September 29, 2005 Declaration"). In addition, there is no teaching or suggestion in the Park publication to use the SL-APC in the assay of the Park publication. Applicants respectfully remind the Examiner that "[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01(III) (citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)) (emphasis original).

Even if, assuming *arguendo*, one of ordinary skill in the art did use SL-APC in the assay disclosed in the Park publication, he/she would not have had an expectation of achieving the result of the claimed method. A skilled artisan would expect a substitute for XL-APC to provide the same result as XL-APC. However, as shown in Example 6 of the specification, the use of SL-APC has an unexpected, improved result over the use of XL-APC. These unexpected results are sufficient to overcome the *prima facie* case of obviousness that the Examiner asserts has been established.

When providing evidence of unexpected results, the evidence should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." M.P.E.P. § 716.02(b)(I) (citing *Ex parte Gelles*, 22 U.S.P.Q.2d 1318, 1319 (Bd. Pat. App. & Inter. 1992)). As discussed in the September 29, 2005 Declaration and during the Examiner interview held on August 2, 2006, the use of SL-APC, as in the claimed method, provides unexpectedly superior results in time-resolved fluorescence assays when compared to the use of XL-APC. This result is unexpected because the substitution of SL-APC for XL-APC in other assays, such as Flow Cytometric Analysis and Immunoassay Analysis, provided similar

results. Therefore, it would have been expected that the results in time-resolved fluorescence assays would also be similar. *See* the September 29, 2005 Declaration, ¶¶ 11-20. Instead, Applicants observed a greater than expected result, *i.e.*, improved results in the claimed time-resolved fluorescence assays. “A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness of the claims at issue.” M.P.E.P. § 716.02(a)(I) (quoting *In re Corkill*, 711 F.2d 1496, 226 U.S.P.Q. 1005 (Fed. Cir. 1985)).

Moreover, Applicants submit herewith a Declaration Under 37 C.F.R. § 1.132 by Mark Wesley Moss (“the Declaration submitted herewith”) providing the results of quality control assays performed on 43 different lots of SL-APC based on the measurement of time-resolved fluorescence. The results were presented during the Examiner interview. The SL-APC used in the quality control assays was prepared by the same method as the SL-APC used in Example 6 of the specification. *See* the Declaration submitted herewith, ¶ 7. The difference in signal-to-noise ratio may be due to variations in the protocol for the time-resolved fluorescence assays of Example 6 and the quality control assay protocol. *See id.* Therefore, any difference in signal-to-noise ratio would be reflected in both the SL-APC and the XL-APC results, (*i.e.*, both have improved signal-to-noise ratio in the quality control assay as compared to Example 6).

The 43 assays performed for quality control purposes provided enough results to perform statistical analysis as requested by the Examiners during the Interview. The statistical analysis proves that the unexpected, improved results obtained by using SL-APC, instead of XL-APC, is statistically significant ($p < 0.05$). *See id.* at ¶ 6. Therefore, when time-resolved fluorescence is measured in an assay using cross-linked APC prepared according to the specification, the resulting signal is unexpectedly greater than the signal from APC cross-linked according to the cited art (*see* September 29, 2005 Declaration, ¶¶ 21-24), and this unexpected difference is statistically significant (*see* the Declaration submitted herewith, ¶ 6), thereby establishing that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance.

Because the prior art neither teaches nor suggests the use of SL-APC in the assay of the Park publication, it does not render the claimed invention obvious. Moreover, since one of ordinary skill in the art would not expect to achieve the claimed invention due to the unexpected results, the claims of the subject application are not obvious over the Park publication. Accordingly, in view of the Remarks set forth above and the Declaration submitted herewith,

reconsideration and withdrawal are respectfully requested with respect to the rejection of claims 3-14 under 35 U.S.C. § 103(a).

The Office Action also rejects claims 11-14 as allegedly being unpatentable over the Park publication and Applicants' statement regarding the sale of product in view of Applicants' admission of prior art. *See* Office Action, p. 4. Applicants respectfully traverse the rejection.

The Examiner has acknowledged that the Park publication and Applicants' statements differ from the claimed invention in failing to teach at least two distinct donor species present in different formats, but asserts that the instant specification discloses that the dye of the invention can be used with any known format for FRET. The Examiner asserts that the it would have been obvious to the skilled artisan to incorporate the cross-linked APC of Applicant into different well known formats of FRET "as disclosed by Applicant" for quantitating an analyte by measuring time resolved fluorescence of a label quantitatively associated with the analyte. *See id.*

Applicants respectfully submit that a *prima facie* case of obviousness cannot be based on Applicants' instant specification. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Rather, both the teaching or suggestion to combine the references and the expectation of success in achieving the claimed invention must be found in the prior art. The deficiencies of the cited prior art have been acknowledged by the Examiner, as the Examiner has stated that the cited art fails to teach at least two distinct donor species present in different formats, as contemplated in claimed embodiments of the invention. These deficiencies cannot be remedied by resort to the instant specification. For this reason, and for the reasons set forth above in response to the rejection of claims 3-10, said remarks being incorporated by reference into the response to the rejection of claim 11-14, Applicants request reconsideration and withdrawal of this rejection.

CONCLUSION

For the reasons set forth above, Applicants respectfully request reconsideration. Applicants believe that incorporation of the amendments and consideration of the above remarks have placed this application in a condition for allowance. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

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